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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,362	MEADE, C.J.M. ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Reply to the Election Requirement filed March 15, 2004 is acknowledged. Applicants have elected with traverse the NK_1 receptor antagonist N-[2-(3,5-bis-trifluoromethylphenyl)ethyl]-2-{4-[3-hydroxypropyl)-methylamino]piperidin-1-yl}-N-methyl-2-phenylacetamide.

The traversal is on the grounds that no indication of further search and examination directed to other species would be performed following an indication of allowable subject matter. Applicants further allege no undue burden is presented.

Applicants' arguments have been given careful consideration but are not found persuasive. Should the elected species found to be free of the prior art, the search will be extended according to current Markush practice. A plethora of structurally distinct compounds are encompassed in instant claim 3, drawn to various NK_1 receptor antagonists. A reasonable number of species is not presented. The search required for one pharmaceutical composition or method of use, with one specific NK_1 receptor antagonist, varies from one antagonist to another. Distinctness is further evidenced by the different classification based on the different structures of the recited antagonists. As to the burden of the search, classification is merely one indication of the burdensome nature of the required search. The literature search of the large number of possible NK_1 receptor antagonists herein claimed is not necessarily co-extensive and is a major factor. Intended use of composition claims confers no patentable weight to the claims. See In re Hack, 112 USPQ 161. Clearly different issues exist and an election of a single disclosed species is proper.

Claims 1-37 are presented.

Accordingly, the subject matter initially under consideration are those pharmaceutical compositions and methods of use wherein a compound of instant formula 1 is in combination with the NK_1 receptor antagonist N-[2-(3,5-bis-trifluoromethylphenyl)ethyl]-2-{4-[3-hydroxypropyl)-methylamino]piperidin-1-yl}-N-methyl-2-phenylacetamide. Other NK_1 receptor antagonists of claims 1-37 are presently withdrawn from consideration by the Examiner, 37 CFR 1.142(b), as directed to non-elected subject matter.

Information Disclosure Statements filed October 9, 2003 and December 18, 2003 are acknowledged. S.N. 10/638769 is not an application of F. Schmidt. Published applications 2002/115680 and 2002/0169181 have been transcribed to the form PTO-1449 filed December 18, 2003, respectively, as U.S. Patent 6,706,726 and U.S. Patent 6,620,438.

A list of co-pending and related applications is requested when Applicants respond to this Office Action.

A Request to add an omitted inventor filed March 8, 2004 is acknowledged. Filing an executed oath/declaration corrects inventorship.

The disclosure is objected to for the following informalities: Applicants are requested to review the specification for proper format and spelling errors. In claim 1, for example, " A Pharmaceutical compositions" should be revised and the recitation "characterized in that they contain" should be replaced with "comprising". It is suggested claim 2 is amended to recite "The pharmaceutical composition according to

claim 1 wherein X^- of formula 1..." Misspellings include "characterized", "stabilizers" and "nebulizing".

Applicants may consider amending claim 21, for example, to recite "The pharmaceutical composition according to claim 20 wherein the inhalable solution or suspension has a pH range of 2-7".

Appropriate correction is required.

In order to provide a complete search of all subject matter presented in claim 4, Applicants are requested to provide the structure of the following compounds: BIIF 1149, CP-122721, FK-888, NKP 608C, NKP 608A, CGP 60829, SR 48968, SR 140333, LY 303 870, MEN-11420, SB 223412, MDL-105172A, MDL-103896, MEN-11149, MEN-11467, DNK 333A, SR-144190, YM-49244, YM-44778, ZM-274773, MEN-10930, S-19752, YM-35275, DA-5018, MK-869, L-754030, CJ-11974, L-758298, DNK-33A, 6b-I, CJ-11974, TAK-637, GR 205171.

Claims 1-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1, 7, 8, 12, 21 and 26 lack clarity with respect to the term "preferably". It is unclear whether or not claims limitations are intended.

The term "general formula" in claims 4 and 5 is indefinite. The term has no probative value.

The recitation in claim 33 "or other principles" is vague and indefinite. The metes and bounds of "other principles" cannot be precisely determined. Applicants should recite those principles contemplated.

The recitations directed to a method of nebulizing in an inhaler according to WO 91/14468 or an inhaler as described in Figures 6a and 6b of WO 97/12687 lack clarity. The specific limitations contemplated that find support in the present specification should be recited.

Claims 4 and 5 are rejected under 35 U.S.C. 112, both first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the invention, and for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

Applicants have failed to particularly point out the definition of "arylglycinamide derivatives of general formula 3". The metes and bounds of said derivatives cannot be precisely determined. Numerous compounds that lack enablement, and an adequate teaching as to how to prepare them, are encompassed in the claims. Undue experimentation would be required to embrace the scope of the claims. Applicants should recite those derivatives contemplated.

Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is directed to the treatment and/or prevention of

any inflammatory or obstructive disease of the respiratory tract. The specification provides support for a capsule formulation of N-[2-(3,5-bis-trifluoromethylphenyl)ethyl]-2-{4-[3-hydroxypropyl)-methylamino]piperidin-1-yl}-N-methyl-2-phenylacetamide. No support is provided for the combination of the compound referenced *supra* and any compound of instant formula 1 for the treatment or prevention of any inflammatory or obstructive disease of the respiratory tract.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment or prevention of any inflammatory or obstructive disease of the respiratory tract.

The relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the field of pulmonology.

Each particular disease or disorder of the respiratory tract has its own specific characteristics and etiology. The unpredictability observed with single agent therapy is compounded when a combination of agents is employed. The broad recitation "treating or preventing any inflammatory or obstructive disease of the respiratory tract" is inclusive of many conditions that presently have no established successful therapies.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any disease and disorder of the respiratory tract.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples to support a treatment modality comprising administering the claimed drug combination.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular diseases would be preferred for treatment or prevention. The skilled artisan would expect the

interaction of a particular combination of drugs in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such parameters. Even for the elected drug combination, no direction is provided with respect to dosages and dosing regimens. Absent reasonable *a priori* expectations of success for using a particular chemotherapeutic combination to treat any particular respiratory tract disease, one skilled in the pulmonology art would have to test extensively many disease states to discover which respond to that claimed combination. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of Pairet et al., U.S. Patent No. 6,455,524 in view of Banholzer et al., S.N. 10/391735.

Pairet teaches the administration of pharmaceutical compositions comprising anticholinergics and NK_1 receptor antagonists for use in the treatment of respiratory tract diseases. Both the dosage forms and NK_1 receptor antagonists are those presently claimed. The anticholinergic agent, tiotropium, is not encompassed in instant formula 1. However, the same anticholinergics of formula 1 are disclosed in pharmaceutical compositions in the co-pending application. The open language of the present claims allows the inclusion of any number of additional active ingredients.

Meade et al., WO 02/069944, is cited to show further the state of the art with respect to pharmaceutical compositions comprising combinations having oxitropium, a bronchodilator of close structural similarity to compounds of instant formula 1, and NK_1 receptor antagonists that are presently claimed for use in the treatment of respiratory tract diseases.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis G. Spivack at telephone number 571-272-0585.

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

May 29, 2004

PHYLLIS SPIVACK
PRIMARY EXAMINER